

# The catalystic asymmetric synthesis of optically active epoxy ketones

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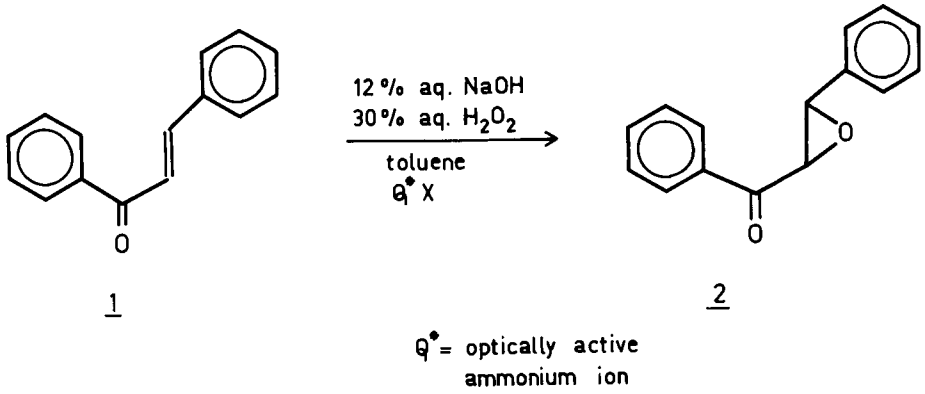
# S U M M A R Y

In this thesis the use of catalytic asymmetric synthesis to prepare optically active epoxy ketones is described. This means that the auxiliary chirality, necessary to obtain an optically active product, is added in a catalytic quantity. In principle this is a very efficient way to make optically active compounds.

In chapter 1 a general introduction is given to asymmetric synthesis; the phase transfer reaction and a number of epoxidation methods are discussed.

In chapter 2 asymmetric phase transfer epoxidation is treated in detail. This chapter is mainly based on the asymmetric epoxidation of chalcone 1, as is shown in scheme 1. The achiral ammonium salts, which are normally used

scheme 1.

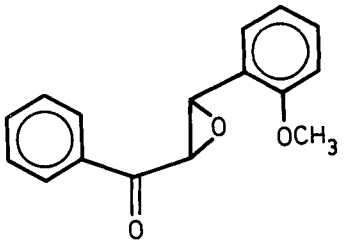



1 2

Q* = optically active ammonium ion

as catalysts in phase transfer reactions, are replaced in our work by optically active ammonium salts, chiefly salts of quinine. In this manner optically active epoxy ketones are obtained. The enantiomeric excess (e.e.) of chalcone epoxide 2 is about 35 % for optimal reaction conditions. When either or both of the phenyl rings in the chalcone 1 carry substituents, chirally catalyzed epoxidation again leads to chiral epoxy ketones. A maximum e.e. of 55 % was obtained with epoxide 3 under the most favourable reaction conditions.

The influence of changes in solvent, temperature, base and catalyst on



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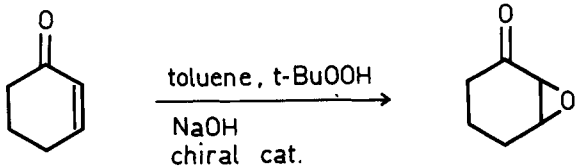
the degree of asymmetric induction under the phase transfer conditions has been investigated in detail and a number of substrates have been epoxidized.

In addition the determination of the absolute configuration of chalcone epoxide is discussed in chapter 2.

In chapter 3 a new method is described to make optically active epoxy ketones. This epoxidation is carried out in an apolar solvent (for example toluene) and the epoxidizing reagent is t-butyl hydroperoxide; a catalytic quantity of base and chiral catalyst is added. The chiral catalyst is an optically active ammonium salt. This reaction has been thoroughly investigated, using the epoxidation of cyclohexenone 4 (scheme 2).

scheme 2.




4 5

In order to obtain the conditions for an optimal asymmetric induction, the reaction conditions have been varied extensively. The highest e.e. obtained for epoxycyclohexanone 5 is 31 % under the reaction conditions mentioned in scheme 2, at $0^{o}C$ and with N,N-dibenzylephedrinium bromide as chiral catalyst. A number of $\alpha,\beta$-unsaturated ketones have been epoxidized and, where possible, their e.e. has been determined.

In addition to the study of the epoxidation, the determination of the absolute configuration of 2,3-epoxycyclohexanone and of benzalacetone epoxide

has been described in chapter 3.

In chapter 4 a theoretical treatment of the circular dichroism of a few epoxy ketones is given. The absolute configuration of epoxycyclohexanone was determined in chapter 3. The enantiomer with the negative rotation has the 2S,3S configuration. In chapter 4 the conformation of a few epoxy ketones is determined. With the aid of these two data the circular dichroism spectrum of epoxycyclohexanone can be explained.

In order to obtain a better insight into the detailed mechanism of these asymmetric epoxidations and in order to be able to predict the absolute configuration of the product, spacefilling molecular models were used as described in chapter 5. Within the limitations of such models an adequate mechanism and reasonable conformations and configurations of the transition states can be proposed.